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# Post-transplant lymphoproliferative disorder and management of residual mass post chemotherapy: Case report



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## ABSTRACT

**INTRODUCTION:** Post-transplant lymphoproliferative disorder (PTLD) is a rare complication. It represents a spectrum of lymphoid proliferations which occur in the setting of immunosuppression and organ transplantation. There are no reported cases or recommendations for the treatment of residual masses post rituximab of PTLD.

**PRESENTATION OF CASE:** A patient with a long standing history of immunosuppression due to multiple kidney transplants starting in 1979, presented with a very large palpable hard abdominal mass (2004) after a fourth renal transplant. There was a past history of heavy immune suppression. CT scans revealed a conglomerate mass involving the right native kidney and two prior right sided renal allografts that crossed the midline. Biopsy of the large right retroperitoneal mass revealed large B cell lymphoma (CD 20 positive); consistent with post-transplant lymphoproliferative disorder (PTLD).

**DISCUSSION:** Management of bulky PTLD, in a highly sensitized, heavily immune suppressed patient is not well described in the literature. The mainstay of therapy is IR and Rituximab (R) monotherapy and combination R-CHOP. CHOP chemotherapy has an associated mortality rate of up to 38%. Radiotherapy is often considered over surgery and surgery has been most frequently used when associated with bowel complications. In this case report we describe upfront Rituximab followed by consolidation resection and cytotoxic chemotherapy as a management strategy to reduce toxicity.

**CONCLUSION:** The approach taken by our surgical team illustrates the benefits of disease debulking in certain cases of PTLD, by guiding further therapy and spacing and reducing chemotherapy in immune suppressed patients.

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## 1. Introduction

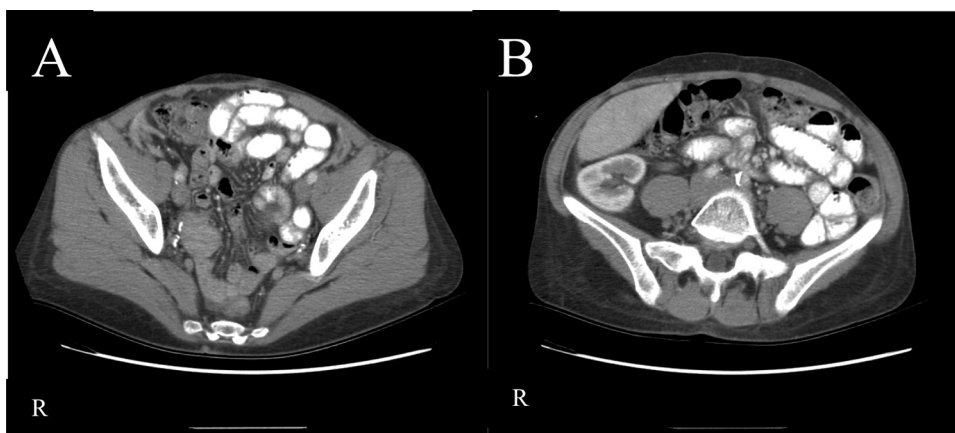
The present work has been structured in line with the SCARE guidelines [1]. Post-transplant lymphoproliferative disorder (PTLD) is a well known albeit rare complication, occurring in approximately 1% of renal transplants [2]. It represents a spectrum of lymphoid proliferations which occur in the setting of immunosuppression and organ transplantation. It is also generally an Epstein-Barr Virus (EBV) associated proliferation ranging from lymphoid hyperplasia to high grade lymphoma and is mostly of B-cell origin. Active EBV infection is associated with the development of PTLD and seronegative transplant recipients who acquire primary EBV infection in the post-transplant period are at an elevated risk of developing PTLD. Mortality of PTLD can be high, but varies between centers and also depends on the type of organ transplanted [3].

Initial treatment of PTLD is immunosuppression reduction (IR). If the disease is localized treatment options include surgery or radiotherapy [4]. However, in the majority of cases PTLD is detected as multifocal disease. Standard treatment includes rituximab, a monoclonal antibody targeted to CD20, alone or in combination with chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Generally, patients will be treated with IR and rituximab monotherapy, and if they fail to respond or have clinically aggressive disease, will be given rituximab + CHOP (R-CHOP) [5]. However, to our knowledge there are no reported cases or recommendations for the treatment of localized residual mass post rituximab of PTLD. We herein describe such a case detailing presentation, therapy and long-term outcome.

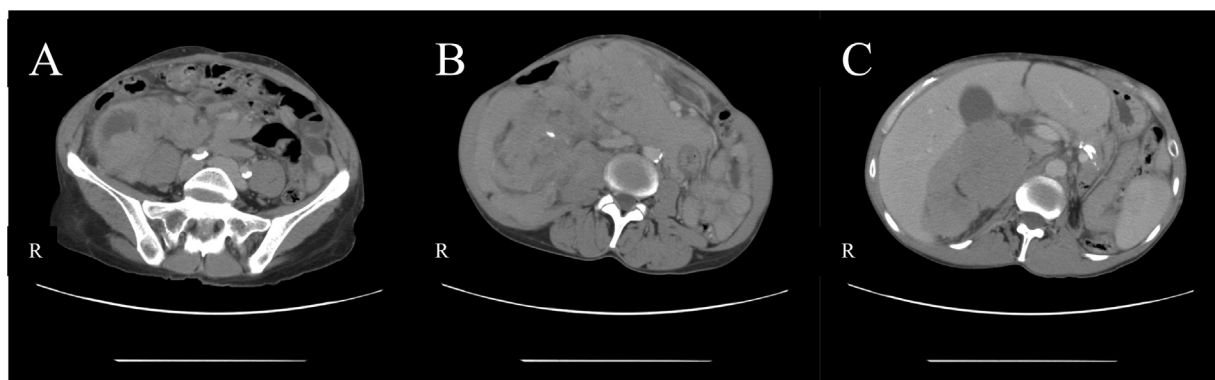
## 2. Case presentation

A 41-year-old female with functioning renal transplantation presented to the University of Alberta Hospital (2004) with increasing diffuse abdominal discomfort, nausea, vomiting, and a palpable abdominal mass. General surgery and the transplant service (urology and nephrology) were consulted.

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**Fig. 1.** An enhances CTscan of the two right sided renal transplants. The patient had an extensive transplant history with both a (A) **Right Iliac Transplant** and a (B) **Right Retroperitoneal Transplant**. Her last transplantation was in 2002 when she received a left sided iliac transplant after a prior left iliac transplant nephrectomy. Both the right sided allografts were non-functional at the time of transplantation in 2002.



**Fig. 2.** A contrast enhanced CT scan of the patient's abdomen at the time of presentation. The mass was found to measure  $13 \times 13 \times 19$  cm on the right side of the abdomen. (A) **Lower Retroperitoneal Mass:** There is demonstrated involvement of a failed right-sided iliac kidney allograft. This appears grossly expanded and distorted. There are cystic regions within the mass that are most likely related to necrosis. (B) **Mid Retroperitoneal Mass:** The mass is causing soft tissue abnormalities within the retroperitoneum at the level of the duodenum and appears to involve the right retroperitoneal renal allograft. (C) **Upper Retroperitoneal Mass:** The liver is homogenous in appearance, with mild intra- and extrahepatic biliary duct dilation. There is mass effect on the pancreas with prominence of the pancreatic duct. Native right kidney is present, atrophic and does not appear to be involved by the mass.

The patient's initial end stage renal disease was of unknown etiology. She had undergone four renal transplants with the first occurring in 1979. The most recent (2002) was a living unrelated allograft placed into the left iliac fossa, with the previous left iliac fossa kidney being removed. The patient also had 2 right non-functioning cadaveric kidneys remaining in her right iliac fossa and retroperitoneum (Fig. 1). Her medical history was significant for having previously been on CellCept and Tacrolimus, and currently on Prednisone, Prograf and Trandate. She was highly sensitized and had two previous courses of OKT3 induction therapy at the time of second and third transplantations. Prior to her most recent renal transplant, she was EBV and CMV positive while the donor was EBV and CMV negative.

The patient was admitted to hospital for further management. A contrast enhanced CT scan revealed a large right sided lower abdominal mass which crossed the midline, and was associated with paracaval lymphadenopathy (Fig. 2). The huge conglomerate of masses in the retroperitoneum measured  $13 \times 13 \times 19$  cm in maximum anterior posterior (AP), transverse and craniocaudal dimensions and had cystic areas, likely related to necrosis. The masses appeared to involve the transplanted kidneys in the right retroperitoneum. The fourth transplant kidney in the left iliac fossa appeared morphologically normal. The atrophic native kidneys appeared otherwise normal. There was a mass effect on the pancreas and liver causing mild pancreatic duct, and intra and

extrahepatic duct dilation. The overall bowel pattern was unremarkable.

An ultrasound guided biopsy of the abdominal mass was performed on the day of admission. The biopsies revealed large cell B cell lymphoma (CD20 positive IHC). Interestingly her EBV viral load was negative. Hematological oncology was consulted and immunosuppression was reduced to single agent Tacrolimus with a target level of  $5\mu\text{g/L}$ . The patient was treated with rituximab (four weekly  $375\text{ mg/m}^2$ ). After 4 cycles of therapy the patient underwent a follow-up CT scan of the abdomen and pelvis revealing marked improvement with significant regression of the mass which now measured  $8.1 \times 7.1$  cm in maximum AP and transverse dimensions (Fig. 3). The largest mass persisted in the right retroperitoneum in the region of the previously transplanted kidney, and was felt to be consistent with residual PTLD. Urology was consulted to determine whether resection of the residual mass would be appropriate.

After 4 more cycles of rituximab the patient underwent another repeat CT scan of the chest, abdomen and pelvis (Fig. 4). There was significant improvement of the retroperitoneal tumors and the two failed renal transplants in the right flank with large tumors associated with them had markedly regressed. The AP, transverse and cradiocaudal dimensions were approximately  $7.0 \times 7.0 \times 10$  cm. There were a few additional solid lesions at the medial aspect of these transplant kidneys, which had also markedly regressed, representing residual disease in enlarged lymph nodes (Fig. 5).

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